

## SUPPORTING INFORMATION

Mass Spectrometry-based Protein Footprinting Characterizes the Structures of Oligomeric Apolipoprotein E2, E3, and E4, Brian Gau, Kanchan Garai, Carl Frieden, Michael L. Gross

**Supporting Information Table 1:** FPOP labeling yield per ApoE residue, WT experiment

residue	ApoE2	ApoE3	ApoE4	residue	ApoE2	ApoE3	ApoE4
V2	0.30 ± 0.05%	0.269 +/- 0.005%	0.29 +/- 0.03%	P183	0.13 +/- 0.02%	0.091 +/- 0.003%	0.13 +/- 0.01%
V6	0.4 +/- 0.1%	0.38 +/- 0.01%	0.41 +/- 0.05%	L184	0.43 +/- 0.07%	0.42 +/- 0.01%	0.43 +/- 0.03%
P10	0.8 +/- 0.1%	0.74 +/- 0.02%	0.81 +/- 0.07%	V185	0.20 +/- 0.03%	0.142 +/- 0.003%	0.21 +/- 0.02%
E13	0.31 +/- 0.02%	0.32 +/- 0.01%	0.32 +/- 0.02%	R191	0.27 +/- 0.03%	0.283 +/- 0.009%	0.31 +/- 0.01%
L14	0.24 +/- 0.04%	0.192 +/- 0.008%	0.18 +/- 0.01%	V195	0.23 +/- 0.04%	0.208 +/- 0.005%	0.25 +/- 0.03%
W20	3.9 +/- 0.5%	3.6 +/- 0.2%	3.9 +/- 0.3%	L198	0.45 +/- 0.08%	0.40 +/- 0.02%	0.42 +/- 0.05%
Q21	4.1 +/- 0.2%	3.8 +/- 0.3%	3.4 +/- 0.2%	L203	0.28 +/- 0.04%	0.249 +/- 0.006%	0.28 +/- 0.03%
W26	1.08 +/- 0.07%	1.0 +/- 0.1%	0.74 +/- 0.08%	E205	0.26 +/- 0.02%	0.215 +/- 0.007%	0.198 +/- 0.007%
W34	3.3 +/- 0.4%	2.9 +/- 0.2%	3.4 +/- 0.4%	W210	3.4 +/- 0.3%	3.5 +/- 0.1%	4.2 +/- 0.5%
M64	10 +/- 2%	9.4 +/- 0.9%	6 +/- 1%	M218	1.0 +/- 0.8%	0.8 +/- 0.4%	1.0 +/- 0.2%
E66	0.0 +/- 0.4%	0.6 +/- 0.2%	0.2 +/- 0.5%	R226	0.12 +/- 0.02%	0.121 +/- 0.003%	0.144 +/- 0.009%
M68	2.5 +/- 0.9%	3.6 +/- 0.6%	2 +/- 1%	K233	0.042 +/- 0.007%	0.047 +/- 0.006%	0.066 +/- 0.006%
Y74	2.8 +/- 0.1%	3.07 +/- 0.04%	3.08 +/- 0.08%	L243	0.09 +/- 0.02%	0.079 +/- 0.006%	0.09 +/- 0.01%
E77	1.47 +/- 0.07%	1.41 +/- 0.04%	1.34 +/- 0.04%	E244	0.067 +/- 0.009%	0.067 +/- 0.005%	0.061 +/- 0.003%
E79	0.18 +/- 0.02%	0.20 +/- 0.02%	0.20 +/- 0.02%	Q248	0.14 +/- 0.02%	0.15 +/- 0.01%	0.15 +/- 0.02%
L82	0.15 +/- 0.03%	0.13 +/- 0.01%	0.13 +/- 0.02%	L252	0.5 +/- 0.1%	0.38 +/- 0.01%	0.37 +/- 0.01%
P84	0.29 +/- 0.05%	0.279 +/- 0.009%	0.31 +/- 0.03%	E255	0.37 +/- 0.01%	0.30 +/- 0.02%	0.250 +/- 0.002%
V85	0.11 +/- 0.03%	0.108 +/- 0.008%	0.113 +/- 0.009%	F257	0.5 +/- 0.6%	1.5 +/- 0.2%	0.9 +/- 0.6%
E87	0.12 +/- 0.02%	0.12 +/- 0.01%	0.12 +/- 0.02%	R260	0.034 +/- 0.006%	0.033 +/- 0.001%	0.036 +/- 0.003%
E88	0.30 +/- 0.07%	0.31 +/- 0.02%	0.33 +/- 0.03%	W264	11 +/- 1%	10.4 +/- 0.4%	10.6 +/- 0.6%
M108	0.0 +/- 0.7%	0.0 +/- 0.5%	5 +/- 1%	E266	0.38 +/- 0.01%	0.340 +/- 0.005%	0.299 +/- 0.006%
C112	22 +/- 5%	26 +/- 1%		D271	0.91 +/- 0.06%	1.03 +/- 0.09%	0.77 +/- 0.05%
M125	10 +/- 3%	12 +/- 1%	9 +/- 2%	M272	6 +/- 3%	9 +/- 3%	5 +/- 2%
L126	0.14 +/- 0.03%	0.16 +/- 0.01%	0.20 +/- 0.02%	W276	6.7 +/- 0.9%	5.8 +/- 0.2%	5.9 +/- 0.3%
L133	0.11 +/- 0.02%	0.102 +/- 0.005%	0.13 +/- 0.01%	V287	0.15 +/- 0.03%	0.134 +/- 0.005%	0.13 +/- 0.02%
H140	6 +/- 2%	6.2 +/- 0.5%	7 +/- 3%	P293	2.0 +/- 0.6%	2.2 +/- 0.1%	1.9 +/- 0.4%
Y162	n.d.	0.75 +/- 0.01%	0.90 +/- 0.02%	P295	0.00 +/- 0.05%	0.08 +/- 0.04%	0.02 +/- 0.06%
L181	0.21 +/- 0.04%	0.141 +/- 0.002%	0.19 +/- 0.02%	H299	1.2 +/- 0.3%	1.08 +/- 0.06%	1.2 +/- 0.3%

**Supporting Information Table 2:** FPOP labeling yield per ApoE residue, oligomer/monomer experiment

residue	ApoE3	ApoE3MM	residue	ApoE3	ApoE3MM	residue	ApoE3	ApoE3MM
K1	2.6 +/- 0.7%	3.6 +/- 0.1%	R90	0.12 +/- 0.06%	0.256 +/- 0.008%	R191	0.2 +/- 0.1%	0.60 +/- 0.04%
E3	0.4 +/- 0.1%	0.47 +/- 0.02%	K95	1.7 +/- 0.6%	2.9 +/- 0.2%	V195	0.5 +/- 0.2%	1.09 +/- 0.04%
V6	0.32 +/- 0.09%	0.36 +/- 0.01%	M108	1 +/- 3%	5. +/- 1%	S197	0.07 +/- 0.02%	0.083 +/- 0.003%
E9	0.18 +/- 0.07%	0.24 +/- 0.02%	C112	53 +/- 12%	54 +/- 6%	L198	0.5 +/- 0.1%	1.13 +/- 0.04%
E19	0.07 +/- 0.01%	0.08 +/- 0.01%	V116	0.24 +/- 0.09%	0.37 +/- 0.02%	Q201	0.010 +/- 0.002%	0.016 +/- 0.001%
W20	11 +/- 3%	16.0 +/- 0.4%	Y118	0.24 +/- 0.09%	0.37 +/- 0.02%	P202	0.18 +/- 0.05%	0.351 +/- 0.005%
Q21	0.07 +/- 0.01%	0.08 +/- 0.01%	V122	0.2 +/- 0.1%	0.12 +/- 0.01%	L203	0.7 +/- 0.2%	1.67 +/- 0.05%
S22	0.052 +/- 0.006%	0.070 +/- 0.006%	M125	50 +/- 5%	47 +/- 5%	E205	0.4 +/- 0.1%	0.84 +/- 0.02%
W26	0.8 +/- 0.2%	1.1 +/- 0.2%	L126	2 +/- 1%	2.0 +/- 0.1%	W210	6 +/- 2%	16.4 +/- 0.4%
L28	0.4 +/- 0.1%	0.53 +/- 0.05%	L133	0.3 +/- 0.2%	0.184 +/- 0.007%	M218	9 +/- 2%	22 +/- 3%
R32	0.023 +/- 0.007%	0.042 +/- 0.004%	H140	1.3 +/- 0.4%	2.0 +/- 0.2%	V232	0.08 +/- 0.03%	4.7 +/- 0.6%
W34	11 +/- 2%	14.2 +/- 0.2%	V161	0.15 +/- 0.05%	0.20 +/- 0.03%	K233	0.10 +/- 0.08%	0.389 +/- 0.004%
Y36	1.3 +/- 0.2%	1.65 +/- 0.08%	Y162	1.6 +/- 0.4%	1.92 +/- 0.05%	K242	0.29 +/- 0.08%	0.55 +/- 0.01%
M64	3.4 +/- 0.9%	3 +/- 1%	A166	0.05 +/- 0.01%	0.076 +/- 0.006%	L243	0.05 +/- 0.02%	1.06 +/- 0.06%
M68	4 +/- 1%	2 +/- 1%	R167	0.25 +/- 0.04%	0.40 +/- 0.01%	E244	0.30 +/- 0.05%	0.49 +/- 0.02%
Y74	4. +/- 1%	3.8 +/- 0.7%	S175	0.13 +/- 0.04%	0.27 +/- 0.02%	Q248	0.18 +/- 0.03%	0.25 +/- 0.02%
E77	0.3 +/- 0.2%	0.22 +/- 0.02%	R180	0.20 +/- 0.05%	0.36 +/- 0.02%	I250	0.03 +/- 0.01%	0.68 +/- 0.06%
E79	0.2 +/- 0.1%	0.18 +/- 0.02%	L181	0.31 +/- 0.08%	0.55 +/- 0.04%	R251	0.012 +/- 0.003%	0.027 +/- 0.001%
E80	1.2 +/- 0.8%	0.72 +/- 0.02%	P183	0.36 +/- 0.08%	0.62 +/- 0.02%	E255	0.28 +/- 0.07%	0.124 +/- 0.003%
L82	0.6 +/- 0.5%	0.187 +/- 0.006%	L184	0.4 +/- 0.1%	0.68 +/- 0.04%	R260	0.29 +/- 0.06%	0.26 +/- 0.01%
P84	0.7 +/- 0.3%	0.65 +/- 0.03%	V185	0.33 +/- 0.08%	0.58 +/- 0.01%	M272	40 +/- 6%	33 +/- 2%
V85	0.9 +/- 0.6%	0.47 +/- 0.04%	E186	0.20 +/- 0.05%	0.36 +/- 0.01%	W276	11 +/- 3%	28.7 +/- 0.8%
E87	0.8 +/- 0.3%	0.99 +/- 0.03%	Q187	0.08 +/- 0.02%	0.154 +/- 0.008%	V294	0.9 +/- 0.2%	0.24 +/- 0.03%
E88	0.7 +/- 0.3%	0.82 +/- 0.03%	R189	0.19 +/- 0.04%	0.34 +/- 0.02%	H299	0.9 +/- 0.4%	2.30 +/- 0.05%

**Supporting Information Table 3:** GEE labeling yield per ApoE residue, oligomer/monomer experiment

residue	time (min)	ApoE3	ApoE3MM	residue	time (min)	ApoE3	ApoE3MM
E7	1	5.19 +/- 0.06%	5.1 +/- 0.4%	E66	1	0.214 +/- 0.008%	0.217 +/- 0.004%
E7	3	6.3 +/- 0.3%	9.0 +/- 0.8%	E66	3	0.29 +/- 0.02%	0.34 +/- 0.09%
E7	6	8.5 +/- 0.8%	9.0 +/- 0.8%	E66	6	0.44 +/- 0.08%	0.32 +/- 0.05%
E7	12	10.6 +/- 0.3%	12.9 +/- 0.7%	E66	12	0.6 +/- 0.1%	0.59 +/- 0.04%
E9	1	4.6 +/- 0.6%	4.6 +/- 0.9%	E77	1	0.7 +/- 0.3%	0.5 +/- 0.2%
E9	3	5.91 +/- 0.08%	9.0 +/- 0.2%	E77	3	0.52 +/- 0.02%	2 +/- 1%
E9	6	9 +/- 1%	9.3 +/- 0.8%	E77	6	1.1 +/- 0.1%	0.6 +/- 0.1%
E9	12	10.9 +/- 0.3%	12.1 +/- 0.1%	E77	12	1.4 +/- 0.1%	1.03 +/- 0.03%
E11	1	0.17 +/- 0.04%	0.135 +/- 0.006%	E80	1	2.2 +/- 0.6%	2.1 +/- 0.3%
E11	3	0.16 +/- 0.01%	0.35 +/- 0.01%	E80	3	2.5 +/- 0.1%	4.2 +/- 0.8%
E11	6	0.37 +/- 0.02%	0.41 +/- 0.01%	E80	6	4.9 +/- 0.8%	4.0 +/- 0.5%
E11	12	0.9 +/- 0.6%	0.7 +/- 0.3%	E80	12	7.3 +/- 0.3%	6.3 +/- 0.1%
E13	1	1.67 +/- 0.07%	1.5 +/- 0.2%	E88	1	0.08 +/- 0.06%	0.04 +/- 0.04%
E13	3	1.98 +/- 0.04%	2.92 +/- 0.07%	E88	3	0.021 +/- 0.003%	0.2 +/- 0.2%
E13	6	3.2 +/- 0.5%	2.9 +/- 0.3%	E88	6	0.084 +/- 0.008%	0.021 +/- 0.009%
E13	12	3.63 +/- 0.06%	4.3 +/- 0.2%	E88	12	0.075 +/- 0.008%	0.041 +/- 0.002%
E19	1	2.9 +/- 0.1%	3.2 +/- 0.2%	E96	1	0.26 +/- 0.04%	0.29 +/- 0.07%
E19	3	4.18 +/- 0.08%	4.1 +/- 0.2%	E96	3	0.405 +/- 0.009%	0.35 +/- 0.07%
E19	6	5.7 +/- 0.4%	4.93 +/- 0.02%	E96	6	0.55 +/- 0.09%	0.3043 +/- 0.0003%
E19	12	10 +/- 2%	7.6 +/- 0.5%	E96	12	0.9 +/- 0.3%	0.35 +/- 0.04%
E27	1	0.3 +/- 0.1%	0.26 +/- 0.04%	E109	1	0.11 +/- 0.01%	0.10 +/- 0.04%
E27	3	0.30 +/- 0.02%	0.37 +/- 0.02%	E109	3	0.21 +/- 0.03%	0.09 +/- 0.09%
E27	6	0.51 +/- 0.02%	0.43 +/- 0.04%	E109	6	0.13 +/- 0.08%	0.16 +/- 0.07%
E27	12	0.62 +/- 0.02%	0.67 +/- 0.07%	E109	12	0.37 +/- 0.09%	0.3 +/- 0.2%
D35	1	0.07 +/- 0.02%	0.052 +/- 0.009%	D110	1	0.11 +/- 0.01%	0.10 +/- 0.04%
D35	3	0.069 +/- 0.003%	0.106 +/- 0.005%	D110	3	0.21 +/- 0.03%	0.09 +/- 0.09%
D35	6	0.16 +/- 0.04%	0.098 +/- 0.006%	D110	6	0.13 +/- 0.08%	0.16 +/- 0.07%
D35	12	0.16 +/- 0.02%	0.14 +/- 0.02%	D110	12	0.37 +/- 0.09%	0.3 +/- 0.2%
E66	1	0.214 +/- 0.008%	0.217 +/- 0.004%	E186	1	0.75 +/- 0.02%	0.75 +/- 0.02%
E66	3	0.29 +/- 0.02%	0.34 +/- 0.09%	E186	3	0.94 +/- 0.02%	0.99 +/- 0.02%
E66	6	0.44 +/- 0.08%	0.32 +/- 0.05%	E186	6	1.3 +/- 0.1%	1.22 +/- 0.02%
E66	12	0.6 +/- 0.1%	0.59 +/- 0.04%	E186	12	1.9 +/- 0.2%	1.9 +/- 0.3%
E77	1	0.7 +/- 0.3%	0.5 +/- 0.2%	E205	1	0.4 +/- 0.1%	0.5 +/- 0.2%
E77	3	0.52 +/- 0.02%	2 +/- 1%	E205	3	0.46 +/- 0.03%	1.0 +/- 0.1%
E77	6	1.1 +/- 0.1%	0.6 +/- 0.1%	E205	6	0.8 +/- 0.1%	0.93 +/- 0.02%
E77	12	1.4 +/- 0.1%	1.03 +/- 0.03%	E205	12	1.04 +/- 0.05%	1.13 +/- 0.07%

E212	1	0.56 +/- 0.01%	1.7 +/- 0.3%	E255	1	0.302 +/- 0.008%	1.3 +/- 0.3%
E212	3	0.97 +/- 0.05%	2.1 +/- 0.2%	E255	3	0.3538 +/- 0.0009%	1.41 +/- 0.07%
E212	6	1.26 +/- 0.08%	2.5 +/- 0.3%	E255	6	0.404 +/- 0.004%	1.8 +/- 0.1%
E212	12	1.9 +/- 0.4%	3.2 +/- 0.2%	E255	12	0.523 +/- 0.009%	2.4 +/- 0.3%
E219	1	2.2 +/- 0.5%	14 +/- 4%	E266	1	8 +/- 3%	3.1 +/- 0.4%
E219	3	4.4 +/- 0.4%	24 +/- 3%	E266	3	8.14 +/- 0.04%	5.5 +/- 0.8%
E219	6	4.7 +/- 0.2%	20 +/- 2%	E266	6	12 +/- 9%	6.3 +/- 0.2%
E219	12	11 +/- 5%	26.2 +/- 0.8%	E266	12	11 +/- 3%	8.23 +/- 0.08%
E220	1	5 +/- 1%	16 +/- 6%	E270	1	12 +/- 8%	1.4 +/- 0.2%
E220	3	8.4 +/- 0.9%	26 +/- 4%	E270	3	4 +/- 3%	2.4 +/- 0.2%
E220	6	9.5 +/- 0.7%	21 +/- 2%	E270	6	9 +/- 6%	2.8 +/- 0.2%
E220	12	19 +/- 8%	25. +/- 1.%	E270	12	1.9 +/- 0.9%	4.20 +/- 0.04%
D227	1	2.2 +/- 0.4%	8 +/- 2%	D271	1	0.05 +/- 0.05%	1.40 +/- 0.07%
D227	3	4.5 +/- 0.5%	17 +/- 5%	D271	3	0.02 +/- 0.02%	2.3 +/- 0.1%
D227	6	6.0 +/- 0.3%	13 +/- 2%	D271	6	0.03 +/- 0.03%	2.8 +/- 0.2%
D227	12	12 +/- 5%	17.42 +/- 0.04%	D271	12	0.2 +/- 0.2%	3.79 +/- 0.07%
E231	1	1.4 +/- 0.3%	10 +/- 3%	E281	1	0.97 +/- 0.06%	1.7 +/- 0.2%
E231	3	3.1 +/- 0.5%	19 +/- 2%	E281	3	1.28 +/- 0.02%	2.3 +/- 0.2%
E231	6	5.1 +/- 0.3%	17 +/- 2%	E281	6	1.70 +/- 0.04%	2.888 +/- 0.006%
E231	12	9 +/- 4%	21 +/- 2%	E281	12	2.3 +/- 0.2%	4.1 +/- 0.2%
E234	1	32 +/- 5%	34 +/- 10%	E287	1	0.3 +/- 0.3%	2.2 +/- 0.1%
E234	3	45.3 +/- 0.6%	45 +/- 3%	E287	3	0	2.95 +/- 0.03%
E234	6	52 +/- 3%	39 +/- 3%	E287	6	0.01 +/- 0.01%	3.9 +/- 0.1%
E234	12	64 +/- 8%	45.4 +/- 0.4%	E287	12	0	5.9 +/- 0.2%
E238	1	3.8 +/- 0.4%	9.1 +/- 0.2%	D297	1	1.4 +/- 0.2%	0.64 +/- 0.03%
E238	3	5.2 +/- 0.3%	11 +/- 2%	D297	3	2.14 +/- 0.06%	0.976 +/- 0.005%
E238	6	6.4 +/- 0.4%	14.9 +/- 0.4%	D297	6	3.49 +/- 0.03%	1.47 +/- 0.08%
E238	12	8.93 +/- 0.05%	18.2 +/- 0.2%	D297	12	5.17 +/- 0.04%	2.315 +/- 0.002%
E244	1	0.086 +/- 0.001%	0.64 +/- 0.04%	H299	1	0.011 +/- 0.008%	0.22 +/- 0.01%
E244	3	0.108 +/- 0.009%	0.72 +/- 0.02%	H299	3	0.023 +/- 0.005%	0.28 +/- 0.01%
E244	6	0.129 +/- 0.004%	0.930 +/- 0.009%	H299	6	0.042 +/- 0.008%	0.39 +/- 0.02%
E244	12	0.164 +/- 0.005%	1.39 +/- 0.08%	H299	12	0.2 +/- 0.1%	0.68 +/- 0.05%
E245	1	0.41 +/- 0.04%	0.91 +/- 0.04%				
E245	3	0.49 +/- 0.02%	1.08 +/- 0.03%				
E245	6	0.58 +/- 0.01%	1.24 +/- 0.03%				
E245	12	0.69 +/- 0.06%	1.97 +/- 0.04%				